

## CLAIMS

- 10 1. A biocompatible microparticle intended to be inhaled, comprising at least one active principle and at least one layer coating this active principle, which is the external layer of said microparticle, said external layer containing at least one coating agent, characterized in that said microparticle has a mean diameter of between 1  $\mu\text{m}$  and 30  $\mu\text{m}$  and an apparent density of between 0.02  $\text{g/cm}^3$  and 0.8  $\text{g/cm}^3$ , and in that it is possible for it to be obtained according to a method comprising the essential steps which are bringing together a coating agent and an active principle and introducing a supercritical fluid, with stirring in a closed reactor.
- 20 2. The microparticle as claimed in claim 1, characterized in that it has a mean diameter of between 1  $\mu\text{m}$  and 15  $\mu\text{m}$ , and even more preferably of between 2  $\mu\text{m}$  and 10  $\mu\text{m}$ , and an apparent density of between 0.05  $\text{g/cm}^3$  and 0.4  $\text{g/cm}^3$ , and in that the active principle/coating agent mass ratio of this particle is between 95/5 and 5/95.
- 25 3. The microparticle as claimed in claim 1 or 2, which can be obtained using a method comprising the following steps:
- 30 - suspending an active principle in a solution of at least one substantially polar coating agent in an organic solvent, said active principle being insoluble in the organic solvent,
- 35 said substantially polar coating agent being insoluble in a fluid in the supercritical state,
- said organic solvent being soluble in a fluid

10049185-0208002

SAD  
A521

in the supercritical state,

- bringing the suspension into contact with a fluid in the supercritical state, so as to desolvate in a controlled way the substantially polar coating agent and ensure its coacervation,
- substantially extracting the solvent using a fluid in the supercritical state and discharging the SC fluid/solvent mixture,
- recovering the microparticles.

5  
A2  
10 *cut*

4. The microparticle as claimed in claim 1 or 2, which can be obtained using a method which consists in suspending an active principle in a supercritical fluid containing at least one coating agent dissolved therein, and then in ensuring the coacervation of the particles by physicochemical modification of the environment.

5. The microparticle as claimed in claim 3, characterized in that the coating agent is chosen from the group made up of

- biodegradable (co)polymers of  $\alpha$ -hydroxy-carboxylic acids, in particular homopolymers and copolymers of lactic acid and glycolic acid, and more particularly PLAs (poly-L-lactide) and PLGAs (poly(lactic-co-glycolic acid)),
- amphiphilic block polymers of the poly(lactic acid)-poly(ethylene oxide) type,
- biocompatible polymers of the poly(ethylene glycol), poly(ethylene oxide) type,
- polyanhydrides, poly(ortho esters), poly- $\epsilon$ -caprolactones and derivatives thereof,
- poly( $\beta$ -hydroxybutyrate), poly(hydroxyvalerate) and poly( $\beta$ -hydroxybutyrate-hydroxyvalerate) copolymers,
- poly(malic acid),

10049186-0208002

5  
H2  
Went

- polyphosphazenes,
- block copolymers of the poly(ethylene oxide)-poly(propylene oxide) type,
- poly(amino acids),
- polysaccharides,
- phospholipids such as phosphatidyl glycerols, diphosphatidyl glycerols containing C12 to C18 fatty acid chains (DLPG, DMPG, DPPG, DSPG), phosphatidylcholines, diphosphatidylcholines containing C12 to C18 fatty acid chains (DLPC, DMPC, DPPC, DSPC), diphosphatidylethanolamines containing C12 to C18 fatty acid chains (DLPE, DMPE, DPPE, DSPE), diphosphatidylserine containing C12 to C18 chains (DLPS, DMPS, DPPS, DSPS), and mixtures which contain the phospholipids mentioned,
- fatty acid esters such as glyceryl stearates, glyceryl laurate, cetyl palmitate, or mixtures which contain these compounds,
- mixtures which contain the abovementioned compounds.

10

15

20

25

30

35

6. The microparticle as claimed in claim 4, characterized in that the coating agent is chosen from the group made up of

- phospholipids such as phosphatidyl glycerols, diphosphatidyl glycerols containing C12 to C18 fatty acid chains (DLPG, DMPG, DPPG, DSPG), phosphatidylcholines, diphosphatidylcholines containing C12 to C18 fatty acid chains (DLPC, DMPC, DPPC, DSPC), diphosphatidylethanolamines containing C12 to C18 fatty acid chains (DLPE, DMPE, DPPE, DSPE), diphosphatidylserine containing C12 to C18 chains (DLPS, DMPS, DPPS, DSPS), and mixtures which contain the phospholipids mentioned,
- mono-, di-, triglycerides in which the fatty acid chains range from C4 to C22, and mixtures

containing them,

- mixtures of glycerides and of esters of polyethylene glycol,
- cholesterol,
- fatty acid esters such as glyceryl stearates, glyceryl laurate or cetyl palmitate,
- biodegradable or bioerodible polymers soluble in a supercritical fluid,
- mixtures which contain the abovementioned compounds.

5  
AZ  
Woff

10

7. The microparticle as claimed in any one of claims 1 to 6, characterized in that the active principle is chosen from the group made up of proteins and peptides, such as insulin, calcitonin, or analogues of the hormone LH-RH, polysaccharides such as heparin, anti-asthmatic agents, such as budesonide, beclometasone dipropionate and its active metabolite beclometasone 17-monopropionate, beta-estradiol hormones, testosterone, broncho-dilators such as albuterol, cytotoxic agents, corticoids, antigens and DNA fragments.

15

20

8. The microparticle as claimed in claim 2, characterized in that the microparticle is an immediate-release microparticle and that the active principle/coating agent mass ratio of this particle is between 95/5 and 80/20.

25

9. A method for preparing microparticles intended to be inhaled, and comprising the following steps:

30

- suspending an active principle in a solution of at least one substantially polar coating agent in an organic solvent,
- said active principle being insoluble in the organic solvent,
- said substantially polar coating agent being insoluble in a fluid in the supercritical

35

10049186-020802

state,

said organic solvent being soluble in a fluid in the supercritical state,

5 A2  
W

- bringing the suspension into contact with a fluid in the supercritical state, so as to desolvate in a controlled way the substantially polar coating agent and ensure its coacervation,

10

- substantially extracting the solvent using a fluid in the supercritical state and discharging the SC fluid/solvent mixture,  
- recovering the microparticles.

15

10. A method for preparing microparticles intended to be inhaled, which consists in suspending, with stirring in a closed reactor, an active principle in a supercritical fluid containing at least one coating agent dissolved therein, and then in ensuring the coacervation of the particles by physicochemical modification of the environment.

20

A3

20049186-020800